



Clutton, E. et al. (2017) Pets in clinical trials. *Veterinary Record*, 181(8), pp. 209-210. (doi:[10.1136/vr.j3913](https://doi.org/10.1136/vr.j3913))

This is the author's final accepted version.

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<http://eprints.gla.ac.uk/146924/>

Deposited on: 08 September 2017

Enlighten – Research publications by members of the University of Glasgow
<http://eprints.gla.ac.uk>

We have been concerned for some time with an apparent progressive loss of clarity between acts of veterinary surgery and animal experimentation, particularly with respect to companion animals. Our concerns were heightened by a *Nature* editorial published on the 8th December 2016 entitled, “Pet projects need a helping hand” and subtitled, “Clinical trials with cats and dogs offer great promise for animal and human medicine but risk being stifled by overzealous regulations” (Anon 2016). This article proposed that the EU directive 2010/63 be relaxed so that veterinarians can conduct clinical trials on pet animals.

In the recent editorial, it was suggested that ‘overzealous regulations’ are stifling scientific progress by limiting the use of companion animals in clinical trials of treatments of both human and animal disease. Whilst we accept the possibility of some benefit arising from such studies, we feel *Nature* significantly underestimates the potential for harms to be caused to the animals used. We argue that robust regulation is necessary for clinical trials carried out using companion animals, just as it is for all scientific uses of animals and for human clinical trials. Indeed, ethical oversight for trials on companion animals which involve the potentially competing interests of animals, owners, treating clinicians and trial funders may be in even more need of independent ethical review and oversight than most other forms of animal research.

The editorial suggests that using pets for clinical trials is scientifically more valid because they are the “real McCoy”: they are genetically diverse, develop the disease spontaneously and share the human environment, and therefore reflect the real-life situation for people. This approach ignores many of the problems inherent in studying naturally occurring disease. Robust scientific evidence relies upon targeted research and the selection of an appropriate model. Clinical research has obvious value but because of the very considerable variation between individuals and their respective disease processes, large numbers of cases must be recruited. Many factors may influence disease onset and progression which may be hard to identify and quantify, not least because significant gaps in the medical history are common. Consequently, to produce reliable information, use of clinical cases often requires specialist experimental design and use of complex statistics. There is, therefore, the very real possibility that clinical trials may fail to deliver meaningful outcomes. One of the fundamental purposes of regulation of the use of animals in experiments or clinical trials is the assessment of the likelihood and importance of a successful trial outcome, before the research begins. Where benefit is unlikely to be achieved or is of little clinical significance, the research should not be allowed to proceed. Thus, the regulatory system offers an important test of the quality of the research, which may be especially important for the very kind of research that the *Nature* editorial suggests should not undergo such regulation.

Leaving aside arguments in relation to model validity, similar ethical concerns apply to subjects of research procedures, be they humans, laboratory animals or pets. Clinical trials may have adverse outcomes (or harms) including side effects of the novel potential therapeutic agent, and failure of the novel compound to perform as well as the current standard treatment. Similarly, the use of placebo in trials will at worst deny, and at best delay the recipients’ access to effective therapy. Clearly, there is significant potential for animals enrolled in a clinical trial to suffer more than they would have if they had undergone the standard treatment.

Projects that involve a risk of harm to the participants need to have sound ethical and regulatory oversight. In fact, the existing mechanisms of approving the use of animals in scientific research are well suited to regulating the use of companion animals in clinical trials, consisting, as they do, of an initial weighing of any potential harms to the animals against the anticipated scientific

benefits of the research. In Europe and elsewhere, if the benefits are judged to outweigh the harms the project is allowed to proceed and is followed by ongoing and independent oversight of the research) to ensure that harms are minimised and benefits maximised, and ends with a retrospective assessment of the actual harms and benefits. These processes have established important safeguards for the welfare of animals used in research, and are of vital importance since animal subjects of clinical trials cannot give their informed consent to participate.

There is one other crucial difference between a veterinary and human clinical trial. In all veterinary trials, a decision can be taken to euthanase an animal. This intervention is not just an option, but a legal and moral obligation when suffering becomes excessive. In regulated animal research, it is usual to set an endpoint before the research begins: a level of suffering that cannot be exceeded. If this point is reached, the animal is humanely killed to end its suffering. Euthanasia offers crucial protection for the welfare of all animals used in research. If the subjects of research are people's pets rather than laboratory animals, it is far harder to set an immutable endpoint. In this case, the ultimate decision on the fate of the animal does not rest with objective observers who have a legal responsibility to minimise suffering. It rests instead with the owner and with the veterinary surgeon, who is acting under the direction of the owner (and may also have a vested interest in the clinical trial). The potential for conflicts of interest is clear. Regulation is critical to ensure that animals do not have their suffering prolonged while their owners wait, potentially in vain, for an unproven treatment to save their dying pet.

Whilst undoubtedly adding some regulatory burden, appropriate control of veterinary clinical trials, like all other research on animals, is essential both to ensure animal welfare and also to ensure that research is of high quality.

For research funders, a primary criterion for supporting research that involves animals is that the research has been subject to appropriate ethical review and regulatory oversight. Most funders would not wish to support any work that might cause harm to animals if it had evaded such oversight by dint of a semantic distinction between 'experiments' and 'clinical trials.' A clinical trial is an experiment to test whether a particular treatment is efficacious. Therefore, a clinical trial should be regulated as such.

We do not argue that trials on pets cannot yield promising scientific data, but rather seek to ensure that they are not undertaken without the same objective consideration of harms and benefits that all other experiments on animals undergo. The regulations in the United Kingdom aim to protect the companion animal from the competing interests of the stakeholders in each clinical case, to protect the welfare of the animal, and to ensure that any suffering is minimised without unduly impeding scientific progress. The welfare of companion animals deserves the same degree of protection as the welfare of animals bred explicitly for research.

A handwritten signature in black ink, appearing to read 'Huw Golledge', with a long, sweeping horizontal line underneath.

Dr Huw Golledge, Universities Federation for Animal Welfare, The Old School, Brewhouse Hill, Wheathampstead, Hertfordshire, AL4 8AN, UK



Prof Paul Flecknell, Newcastle University, Newcastle upon Tyne NE1 7RU



Dr Polly Taylor, Taylor Monroe, Gravel Head Farm, Little Downham, Nr Ely, Cambs CB6 2TY



Prof Eddie Clutton, Wellcome Trust Critical Care Laboratory for Large Animals, Roslin Institute, Easter Bush, Midlothian EH25 9RG



Dr Kathy Murphy, Comparative Biology Centre, Newcastle University, NE2 4HH



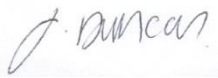
Guen Bradbury, Innovia Technology, St Andrew's House, St Andrew's Road, Cambridge, CB4 1DL



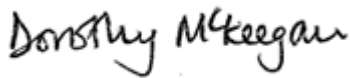
David Chennells, Court Farm, Olney, MK46 5EH



Dr Gabrielle C Musk, Animal Care Services, The University of Western Australia, M720, Perth WA
6009 Australia



Juliet Duncan, Royal (Dick) School of Veterinary Studies, Easter Bush Campus, University of
Edinburgh, EH25 9RG



Dr Dorothy McKeegan, Institute of Biodiversity, Animal Health and Comparative Medicine,
University of Glasgow



Bryony Few, Charles River Laboratories, Tranent, East Lothian, EH33 2NE



Dr Ngaire Dennison, Biological Services, University of Dundee, MSI/WTB/JBC Complex,
Dow Street, Dundee DD1 5EH

References

EDITORIAL (2016) Pet projects need a helping hand. *Nature* 540, 169.

JARVIS, S. (2010) Where do you draw the line on treatment? *Veterinary Record* 167, 636-637